510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY TEMPLATE

A. 510(k) Number:

k123404

B. Purpose for Submission:

The addition of imipenem

C. Measurand:

Imipenem 0.0625-32µg/mL

D. Type of Test:

Antimicrobial Susceptibility Test (AST) colorimetric oxidation-reduction, growth-based

E. Applicant:

Becton, Dickinson & Company

F. Proprietary and Established Names:

BD Phoenix™ Automated Microbiology System- Imipenem 0.0625-32µg/mL

G. Regulatory Information:

1. Regulation section:
   21 CFR 866.1645 - Fully Automated Short-Term Incubation Cycle Antimicrobial Susceptibility System

2. Classification:
   II

3. Product code:
   LON

4. Panel:
   83 Microbiology

H. Intended Use:

1. Intended use(s):

The BD Phoenix Automated Microbiology System is intended for the *in vitro* rapid identification (ID) and quantitative determination of antimicrobial susceptibility by minimal inhibitory concentration (MIC) of Gram Negative aerobic and facultative anaerobic bacteria belonging to the family *Enterobacteriaceae* and non-*Enterobacteriaceae*.

2. Indication(s) for use:

The BD Phoenix™ Automated Microbiology System is intended for *in vitro* quantitative determination of antimicrobial susceptibility by minimal inhibitory concentration (MIC) of most Gram-negative aerobic and facultative anaerobic bacteria isolates from pure culture for *Enterobacteriaceae* and Non-*Enterobacteriaceae* and most Gram-positive bacteria isolates from pure culture belonging to the genera *Staphylococcus, Enterococcus* and *Streptococcus*.

Imipenem has been shown to be active *in vitro* against most strains of microorganisms listed below, as described in the FDA-approved package insert for this antimicrobial agent.

Active *In Vitro* and in Clinical Infections Against:
Acinetobacter spp.
Citrobacter spp.
Enterobacter cloacae
Escherichia coli
Klebsiella spp.
Pseudomonas aeruginosa
Serratia marcescens

3. Special conditions for use statement(s):

For prescription use only

4. Special instrument requirements:

For use with BD Phoenix™ Automated Microbiology System

I. Device Description:

This submission is for the AST Panel only. The ID system was not reviewed.

The BD Phoenix™ Automated Microbiology System includes instrumentation and software, sealed and self-inoculating molded polystyrene trays with 136 micro-wells containing dried reagents, and specific inoculum broth formulations for ID and AST indicator. The organism to be tested must be a pure culture and be preliminarily identified as gram positive or gram negative. Colonies are then suspended in broth, and equated to a 0.5 McFarland with the recommendation to use BD nephelometer devices. A further dilution is made into an AST broth, which turns to blue after AST broth indicator is added prior to inoculating the panel. The AST broth is a cation-adjusted formulation of Mueller-Hinton broth containing 0.01%

Tween 80, and has a final inoculum of approximately 5 x 10^5 CFU/mL. After inoculation and incubation, the color changes to pink then to colorless as reduction in the panel well proceeds. Inoculated panels are barcode scanned and loaded into the BD Phoenix™ Automated Microbiology System instrument where the panels are incubated at 35°C and continuously measured of changes to the indicator as well as bacterial turbidity to determine the bacterial growth in the presence of an antimicrobial agent. Organisms growing in the presence of a given antimicrobial agent reduce the indicator, signaling organism growth and resistance to the antimicrobial agent. Organisms killed or inhibited by a given antimicrobial do not cause reduction of the indicator and therefore do not produce a color change. Additional interpretation is done using software driven "EXPERT" System using rules derived from the CLSI documentation.

Readings are taken every 20 minutes with an AST result available between 4-16 hours. This is only an autoread result; no manual readings are possible with this system.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   VITEK® System

2. Predicate 510(k) number(s):

   N50510

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Intended Use	The BD Phoenix™ Automated Microbiology System is intended for the rapid identification and *in vitro* antimicrobial susceptibility testing of isolates from pure culture of most aerobic and facultative anaerobic Gram-negative and Gram-positive bacteria of human origin.	The VITEK System is intended for the determination of *in vitro* susceptibility to antimicrobial agents for rapidly growing, aerobic and/or facultative anaerobic Gram-negative and Gram-positive bacteria.
Sample	Isolated colonies from culture	Same
Result reported	Minimum inhibitory concentration (MIC) and categorical interpretation (SIR)	Same
Incubation Time	<16 hours	<16 hours
Type of Test	Automated	Same

Differences		
Item	Device	Predicate
Results achieved (MIC)	Serial twofold dilutions of antimicrobial	Computer-assisted extrapolation of doubling dilutions
Technology	Automated growth based enhanced by use of a redox indicator (colorimetric oxidation-reduction) to detect organism growth.	Automated growth based with detection using an attenuation of light measured by an optical scanner.

K. Standard/Guidance Document Referenced (if applicable):

"Class II Special Controls Guidance Document: Antimicrobial Susceptibility Test Systems; Guidance for Industry and FDA"

CLSI M7-A8, "Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically"

CLSI M100, S22 "Performance Standards for Antimicrobial Susceptibility Testing"

L. Test Principle:

The BD Phoenix™ Automated Microbiology System is a broth based microdilution method that utilizes a redox indicator (colorimetric oxidation-reduction) to enhance detection of organism growth. The MIC is determined by comparing growth in wells containing serial two-fold dilutions of an antibiotic to the growth in "growth control wells" which contains no antibiotic.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Eighteen organisms were evaluated at three sites (one internal and two external) in triplicate on three separate days using inoculum prepared manually or by the automated BD Phoenix AP. Inter-site and Intra-site testing demonstrated reproducibility of ≥95%.

b. Linearity/assay reportable range:

Not applicable

c. Traceability, Stability, Expected values (controls, calibrators, or methods):

The FDA and CLSI recommended QC isolates, *E. coli* ATCC 25922 and *P. aeruginosa* ATCC 27853 were used with the reference method and the BD Phoenix™ Automated Microbiology System. Inoculum density was standardized by manual (CrystalSpec or BD PhoenixSpec) or automated (BD Phoenix AP) methods. The BD Phoenix™ was tested sufficient number of times to demonstrate that the system can produce acceptable range results >95% of the time by both inoculum preparation methods.

Imipenem QC Table

ORGANISM	conc. (µg/mL)	Manual (CrystalSpec/ PhoenixSpec)		BD Phoenix™ AP	
		Ref	Phoenix	Ref	Phoenix
E. coli ATCC 25922 Expected Range: ≤0.0625- 0.25µg/mL	≤0.0625				
	0.125	40	30	40	24
	0.25	35	67	35	128
	0.5				
P. aeruginosa ATCC 27853 Expected Range: 1-4 µg/mL	0.25				
	0.5	1		1	
	1	20		20	
	2	51	93	51	82
	4	3	5	3	12
	NC	1			

Inoculum density control: The organism suspension density of the ID broth was standardized using BD nephelometer device which was verified each day of testing. Internal validation data was used to demonstrate that the use of BD nephelometer devices would produce reproducible results.

d. Detection limit:

Not applicable

e. Analytical specificity:

Not applicable

f. Assay cut-off:

Not applicable

2. Comparison studies:

a. Method comparison with predicate device:

The broth dilution reference panel was prepared according to CLSI recommendation and was used to compare with the BD Phoenix™ results. Clinical testing was performed at three sites. The testing included both fresh clinical isolates and stock isolates along with a challenge set with known results. The test device had a growth rate of >95%. A comparison was provided to the reference method with the following agreement.

GP Accuracy Summary Clinical and Challenge

	EA Tot	EA N	EA %	Eval EA Tot	Eval EA N	Eval EA %	CA Tot	CA N	CA %	#R	min	maj	vmj
Clinical	1177	1104	93.8	1123	1051	93.6	1177	1117	94.9	110	56	3	1
Challenge	171	171	100	146	146	100	171	167	97.7	63	4	0	0
Combined	1348	1275	94.6	1269	1197	94.3	1348	1284	95.3	173	60	3	1

EA-Essential Agreement
CA-Category Agreement
R-resistant isolates
maj-major discrepancies
vmj-very major discrepancies
min- minor discrepancies

Essential agreement (EA) is when the BD Phoenix™ panels agree with the reference test panel results exactly or within one doubling dilution of the reference method. Category agreement (CA) is when the BD Phoenix™ panel result interpretation agrees exactly with the reference panel result interpretation. Evaluable EA is when the MIC result is on scale for both the BD Phoenix™ and the reference and have on-scale EA.

The overall performance was acceptable. There was one very major discrepancy with *P. aeruginosa* resulting in an acceptable category agreement of 91.2% when analyzing separately. Of the three major discrepancies, two were from *Enterobacter cloacae* (maj discrepancy rate 2.1%) and one from *E. coli* (maj discrepancy rate 0.2%). The overall vmj rate and maj rate were 0.6% and 0.3% respectively; they were acceptable. In the clinical studies, the trend was more resistant (1 dilution higher) when comparing to the reference for these organisms: *E. coli*, *K. oxytoca*, *K. pneumoniae* and *P. aeruginosa.*

The performance of the BD Phoenix AP was also evaluated in the challenge study with acceptable results:

Comparison challenge Data- Manual and automated Phoenix AP

	EA Tot	EA N	EA %	Eval EA Tot	Eval EA N	Eval EA %	CA Tot	CA N	CA %	#R	min	maj	vmj
Manual	171	171	100	146	146	100	171	167	97.7	63	4	0	0
Phoenix AP	173	171	98.8	148	146	98.6	173	168	97.1	65	5	0	0

b. Matrix comparison:

Not applicable

3. Clinical studies:

   a. Clinical Sensitivity:

   Not applicable

   b. Clinical specificity:

   Not applicable

   c. Other clinical supportive data (when a. and b. are not applicable):

   Not applicable

4. Clinical cut-off:

   Not applicable

5. Expected values/Reference range:

Enterobacteriaceae	≤1, 2, ≥4
Pseudomonas aeruginosa	≤2, 4, ≥8
Acinetobacter spp.	≤4, 8, ≥16

N. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

O. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.